



DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-623]

Schedules of Controlled Substances: Placement of 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-methyltryptamine (5-MeO-AMT), 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (5-MeO-MiPT), 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET), and *N,N*-diisopropyltryptamine (DiPT) in Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing five tryptamine hallucinogens, as identified in this proposed rule, in schedule I of the Controlled Substances Act. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis with, or possess), or propose to handle these five specific controlled substances.

DATES: Comments must be submitted electronically or postmarked on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). The electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period. To ensure proper handling of comments, please reference “Docket No. DEA-623” on all electronic and written correspondence, including any attachments.

- *Electronic comments:* DEA encourages commenters to submit all comments electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the webpage or attach a file for lengthier comments. Please go to <https://www.regulations.gov> and follow the on-line instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number. Submitted comments are not instantaneously available for public view on regulations.gov. If you have received a Comment Tracking Number, you have submitted your comment successfully and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

- *Paper comments:* Paper comments that duplicate electronic submissions are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA FR Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

- *Hearing requests:* All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing

Clerk/OALJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA FR Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

FOR FURTHER INFORMATION CONTACT: Terrence L. Boos, Drug & Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249.

SUPPLEMENTARY INFORMATION: In this proposed rule, the Drug Enforcement Administration (DEA) proposes to schedule the following five controlled substances in schedule I of the Controlled Substances Act (CSA), including their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation:

- 4-Hydroxy-N,N-diisopropyltryptamine (4-OH-DiPT),
- 5-Methoxy-alpha-methyltryptamine (5-MeO-AMT),
- N-Isopropyl-5-Methoxy-N-Methyltryptamine (5-MeO-MiPT),
- N,N-Diethyl-5-methoxytryptamine (5-MeO-DET), and
- N,N-Diisopropyltryptamine (DiPT).

Posting of Public Comments

All comments received in response to this docket are considered part of the public record. DEA will make comments available, unless reasonable cause is given, for public inspection online at <https://www.regulations.gov>. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act applies to all comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want DEA to make it publicly available, you must include the phrase “PERSONAL IDENTIFYING INFORMATION” in the first paragraph of your comment. You must also place all of the personal identifying information you do

not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want DEA to make it publicly available, you must include the phrase “CONFIDENTIAL BUSINESS INFORMATION” in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

DEA will generally make available in publicly redacted from comments containing personal identifying information and confidential business information identified, as directed above. If a comment has so much confidential business information that DEA cannot effectively redact it, DEA may not make available publicly all or part of that comment. Comments posted to <https://www.regulations.gov> may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as confidential as directed above.

An electronic copy of this document and supplemental information to this proposed rule are available at <https://www.regulations.gov> for easy reference.

Request for Hearing or Appearance; Waiver

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act, 5 U.S.C. 551-59. 21 CFR 1308.41 through 1308.45; 21 CFR part 1316, subpart D. Interested persons may file requests for a hearing or notices of intent to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(a) or (b), and such requests must include a statement of interest in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. 21 CFR 1316.47(a). Any interested person may file a waiver of an opportunity

for a hearing or to participate in a hearing together with a written statement regarding the interested person's position on the matters of fact and law involved in any hearing as set forth in 21 CFR 1308.44(c).

All requests for hearing and waivers of participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above.

Legal Authority

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General on his own motion. 21 U.S.C. 811(a). This proposed action was initiated on the Attorney General's own motion, as delegated to the Administrator of DEA (Administrator), and is supported by, *inter alia*, a recommendation from the former Assistant Secretary for Health of the Department of Health and Human Services (former Assistant Secretary of HHS or former Assistant Secretary)¹ and an evaluation of all relevant data by DEA. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to controlled substances, including those specific to schedule I controlled substances, on persons who handle or propose to handle 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT.

Background

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are tryptamine hallucinogens. They share structural and pharmacological similarities with several schedule I tryptamine hallucinogens, such as *alpha*-methyltryptamine (AMT), *N,N*-dimethyltryptamine (DMT), 5-methoxy-*N,N*-diisopropyltryptamine (5-MeO-DiPT), and psilocyn. They have no approved medical use in the United States.

¹The Secretary of HHS has delegated to the Assistant Secretary for Health the authority to make domestic drug scheduling recommendations.

Proposed Determination to Schedule 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT

Pursuant to 21 U.S.C. 811(b), DEA gathered the necessary data on 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT, and on December 19, 2008, submitted it to the former Assistant Secretary with a request for a scientific and medical evaluation of available information and a scheduling recommendation for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT.

On March 29, 2012, May 17, 2012, and August 14, 2012, HHS provided to DEA scientific and medical evaluations for the above mentioned five tryptamines and a scheduling recommendation for each. The evaluations were entitled: 1) “Basis for the Recommendation to Control 4-Hydroxy-N,N-diisopropyltryptamine (4-OH-DIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA);” 2) “Basis for the Recommendation to Control 5-Methoxy-alpha-methyltryptamine (5-MeO-AMT) and its Salts in Schedule I of the Controlled Substances Act (CSA);” 3) “Basis for the Recommendation to Control N-Isopropyl-5-Methoxy-N-Methyltryptamine (5-MeO-MIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA);” 4) “Basis for the Recommendation to Control N,N-Diethyl-5-methoxytryptamine (5-MeO-DET) and its Salts in Schedule I of the Controlled Substances Act (CSA);” and 5) “Basis for the Recommendation to Control N,N-Diisopropyltryptamine (DIPT) and its Salts in Schedule I of the Controlled Substances Act (CSA).” Following consideration of the eight factors and findings related to each of the substances’ abuse potential, legitimate medical use, and dependence liability, HHS recommended that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT and their respective salts be controlled in schedule I of the CSA under 21 U.S.C. 812(b).

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS and all other relevant data, and completed its own

eight-factor review pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA in their respective eight-factor analyses, and as considered by DEA in this proposed scheduling determination. Please note that both DEA and HHS analyses are available in their entirety under “Supporting Documents” of the public docket for this proposed rule at <https://www.regulations.gov> under docket number “DEA-623.”

1. *The Drugs’ Actual or Relative Potential for Abuse:*

In addition to considering the information HHS provided in its scientific and medical evaluation documents for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT, DEA also considered all other relevant data regarding actual or relative potential for abuse of each substance. The term “abuse” is not defined in the CSA, however the legislative history of the CSA suggests the following four prongs in determining whether a particular drug or substance has a potential for abuse:²

- a. Individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community; or*
- b. There is a significant diversion of the drug or other substance from legitimate drug channels; or*
- c. Individuals are taking the drug or other substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs; or*
- d. The drug is so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.*

² Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., 2nd Sess. (1970) reprinted in 1970 U.S.C.A.N. 4566, 4603.

DEA reviewed the scientific and medical evaluation provided by HHS and all other data relevant to the abuse potential of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. These data as presented below demonstrate that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have a high potential for abuse.

a. There is evidence that individuals are taking the drug or other substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community.

According to HHS 2012 review, and more current DEA findings, data show that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have been encountered by law enforcement (Factor 5). Based on published case reports in the medical literature and anecdotal reports (Factor 2), HHS states that these substances are being abused for their hallucinogenic properties. HHS has determined that consumption of these five tryptamines due to their hallucinogenic properties poses a safety hazard to the public health. There were hospital emergency room admissions related to the abuse of 5-MeO-AMT and 5-MeO-MiPT. One confirmed death was reported in 2004 from the abuse of 5-MeO-AMT, taken in combination with alcohol and the antidepressant bupropion; however, it is unclear what role 5-MeO-AMT played in the death.

b. There is significant diversion of the drug or substance from legitimate drug channels.

HHS, in its 2012 review, stated that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not Food and Drug Administration (FDA)-approved drug products for treatment in the United States and that it is unaware of any country in which their use is legal. DEA has confirmed with HHS that their 2012 statements are still applicable. In addition, HHS' 2012 review stated that there appear to be no legitimate sources for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT as marketed drugs. DEA notes that these substances are available for purchase from

legitimate suppliers for scientific research. However, there is no evidence of significant diversion of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT from legitimate suppliers.

c. Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substance.

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not approved for medical use and are not formulated or available for clinical use. Therefore, individuals are taking 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT on their own initiative, rather than based on medical advice from a practitioner licensed by law to administer drugs. This is consistent with the data from law enforcement seizures and case reports suggesting that individuals are taking these substances for similar hallucinogenic effects produced by lysergic acid diethylamide (LSD) and *N,N*-diethyltryptamine (DET), while possibly simultaneously attempting to circumvent criminal prosecution since these are explicitly scheduled substances (*see* Factor 5 for more detailed information).

d. The drug is a new drug so related in its action to a drug or other substance already listed as having a potential for abuse to make it likely that the drug substance will have the same potential for abuse as such drugs, thus making it reasonable to assume that there may be significant diversion from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

After scientific evaluation, HHS states that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are structural analogs of schedule I hallucinogens (4-OH-DiPT of 5-MeO-DiPT, 5-MeO-AMT of AMT, 5-MeO-MiPT of DMT, 5-MeO-DET of 5-MeO-DMT and DMT, and DiPT of 5-MeO-DiPT) and produce similar pharmacological effects to natural and synthetic schedule I hallucinogens.

4-OH-DiPT

4-OH-DiPT elicits pharmacological responses similar to the schedule I substances 4-methyl-2,5-dimethoxy-amphetamine (DOM) and LSD, which have no accepted medical use and have high abuse potential. In animal drug discrimination studies, 4-OH-DiPT fully generalizes for the discriminative stimulus effects of DOM and LSD in rats. Additionally, 4-OH-DiPT produces classic hallucinogenic effects such as perceptual distortions and pleasurable physical effects. Risks and effects of 4-OH-DiPT include: hallucinations, euphoria, fatigue, headache, gastrointestinal distress, insomnia, and anxiety. HHS states that these effects are like those of schedule I hallucinogens and concludes that based on the psychological and cognitive disturbances associated with effects of 4-OH-DiPT, it is reasonable to assume that this substance has a substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-AMT

According to HHS, 5-MeO-AMT elicits pharmacological responses similar to the schedule I substances LSD and DET which have no accepted medical use and have high abuse potential. Drug discrimination data demonstrate that 5-MeO-AMT produces partial generalization for the discriminative stimulus effects of LSD in rats. In humans, 5-MeO-AMT produces hallucinogenic effects similar to those produced by LSD and DET, including euphoria and visual and auditory hallucinations. Adverse effects caused by 5-MeO-AMT are similar to those of schedule I hallucinogens including: fatigue, headache, gastrointestinal distress, insomnia, and anxiety. Based on the hallucinogenic and other effects caused by 5-MeO-AMT, HHS states that it is reasonable to assume that this substance has substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-MiPT

According to HHS, 5-MeO-MiPT elicits pharmacological responses similar to the schedule I substances LSD and DMT, which have no accepted medical use and have high abuse potential. Drug discrimination studies showed that 5-MeO-MiPT fully generalizes to the discriminative stimulus effects of DOM in rats, and partially generalizes to the discrimination stimulus effects of LSD, DMT, and 3,4-methylenedioxy-methamphetamine (MDMA, schedule I). In humans it has been reported that 5-MeO-MiPT is 15-fold more potent than DMT when comparing doses that produce hallucinogenic effects. Thus, HHS concluded that it is reasonable to assume that 5-MeO-MiPT has substantial capability to cause a hazard to public health, both to the user and to the community.

5-MeO-DET

According to HHS, 5-MeO-DET elicits pharmacological responses similar to the schedule I substances DMT and DOM, which have no accepted medical use and have high abuse potential. In animal drug discrimination studies, 5-MeO-DET fully generalizes for the discriminative stimulus effect of DMT in rats. 5-MeO-DET partially generalizes to the discriminative stimulus cues of DOM and MDMA. The reports from users describe the effects of 5-MeO-DET as being similar to those produced by DMT and LSD. Adverse health risks associated with 5-MeO-DET use include: bizarre behavior, hallucinations, and sympathomimetic effects, such as increased heart rate. These adverse effects are similar to those of schedule I hallucinogens. Based on available information, it is reasonable to assume that 5-MeO-DET has substantial capability to cause a hazard to public health, both to the user and to the community.

DiPT

According to HHS, DiPT elicits pharmacological responses similar to the schedule I substances DOM and DMT, which have no accepted medical use and have high abuse potential. Drug discrimination studies showed that DiPT fully substitutes for

the discriminative stimulus effects of DOM and DMT in rats. The reports from users describe the effects of DiPT as being similar to those produced by 4-bromo-2,5-dimethoxyphenethylamine (2C-B), 2-(2,5-dimethoxy-4-methylphenyl)ethanamine (2C-D), and 2,5-dimethoxy-4-ethylamphetamine (DOET), all of which are classified as schedule I substances. Risks associated with DiPT use are based on the perceptual changes in the auditory experience. Like schedule I hallucinogens, DiPT produces adverse effects such as: auditory and other sensory distortions, lethargy, nausea, hyperreflexia, and mydriasis. Based on the adverse effects associated with DiPT, it is reasonable to assume that this substance has substantial capability to cause a hazard to public health, both to the user and to the community.

2. Scientific Evidence of the Drugs' Pharmacological Effects, If Known:

As stated by HHS (HHS reviews, 2012a-e), the neurochemical effects of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT mainly involve serotonergic system in the central nervous system (CNS). Tryptamine hallucinogens are believed to produce their characteristic effects primarily through stimulation of the 2A subtype of serotonin (5-HT) receptors (5-HT_{2A}). DEA further notes that the 5-HT_{2A} receptor has also been shown to mediate the *in vivo* behavioral effects and discriminative stimulus effects of the three classes of classic hallucinogens, ergotamines (e.g., LSD), phenethylamines (e.g., DOM), and tryptamines (e.g., DMT).

Animal testing data in rats show that stimulus properties of 4-OH-DiPT are similar to DOM and LSD, and partially similar to DMT; 5-MeO-AMT substantially overlaps with LSD; 5-MeO-MiPT substantially overlaps with DOM, LSD, and MDMA; 5-MeO-DMT are similar to DMT, DOM, and MDMA; and DiPT are similar to DOM and DMT, and are partially similar to LSD. Thus, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT produce psychopharmacologic effects similar to those produced

by serotonin-mediated hallucinogens in an animal model, which are predictive of its abuse in humans.

In humans, users of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT report hallucinogenic effects similar to LSD and DET including: euphoria, hallucinations involving various senses, perceptual distortions and pleasant intensification of sensory experiences. Physiological and psychological effects have been reported to be frightening or disturbing and can include: dizziness, fatigue, headache, trembling, anxiety, insomnia, restlessness, cold sweats, and gastrointestinal disturbances (i.e., nausea, vomiting, and diarrhea), among others. One death was reported in 2004 with the use of 5-MeO-AMT, however alcohol and bupropion (an antidepressant) were also detected in post mortem toxicology analyses.

3. The State of Current Scientific Knowledge Regarding the Drugs or Other Substances:

Chemistry

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are part of the tryptamine family and share the core tryptamine structure with substitutions at the α -position, 4-position, 5-position, and on the nitrogen (N) atom. All of these substances contain an indole ring with a substituted ethylamino sidechain. 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT share structural similarities with schedule I tryptamine hallucinogens such as DMT, DET, AMT, and psilocyn.

Pharmacokinetics

Metabolism studies have not been conducted for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-DET, and DiPT. However, metabolism has been reported for 5-MeO-MiPT. Similar to other structurally related tryptamines, 5-MeO-MiPT has been reported to undergo metabolism through oxidative deamination, *N*-demethylation, *O*-demethylation, and *N*-oxidation with *N*-oxides as the major metabolites. Thus, it is highly likely that 4-

OH-DiPT, 5-MeO-AMT, 5-MeO-DET, and DiPT will be metabolized in a similar manner.

4. Its History and Current Pattern of Abuse:

In the U.S., law enforcement entities have initially encountered 5-MeO-AMT and DiPT in 2003, 5-MeO-MiPT in 2004, 5-MeO-DET in 2006, and 4-OH-DiPT in 2009, according to the National Forensic Laboratory Information System (NFLIS).³ Each of these tryptamines has been encountered in one or more of the following forms: powder, tablets, capsules, liquid, or on blotter paper. These substances are generally purchased from Internet-based companies in addition to being purchased from dealers. These tryptamines are often misrepresented as LSD to users due to their similarities in producing hallucinogenic effects.

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT do not have an approved medical indication in the U.S. and therefore have no legitimate medical use in the U.S. Anecdotal reports from users of these substances indicate that these substances produce classical hallucinogenic properties, such as perceptual distortions and pleasurable physical effects. Users report oral administration as the most common route of administration. Other routes of administration such as insufflation, smoking, and rectal administration have been reported.

5. The Scope, Duration, and Significance of Abuse:

Tryptamine hallucinogens, both natural and synthetic, have been popular among the attendees of rave parties, music concerts, and other large or social venues, as well as in intimate and smaller settings since the 1990s in the U.S. and Europe. Often these substances are promoted as substitutes for LSD. Synthetic hallucinogens and stimulants

³ NFLIS is a national drug forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by state and local forensic laboratories across the country. The NFLIS participation rate, defined as the percentage of the national drug caseload represented by laboratories that have joined NFLIS, is over 97 percent. NFLIS includes drug chemistry results from completed analyses only.

are known as “club drugs.” In addition to sales in raves and nightclubs, Internet sales have become one of the main outlets for the sale and distribution of tryptamine hallucinogens.

In the U.S., there has been significant availability, trafficking and abuse of a number of tryptamines including 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. This is evidenced by large numbers of encounters of one or more of these tryptamines by U.S. law enforcement in 47 states and the District of Columbia.

According to NFLIS, there have been 5 reports of 4-OH-DiPT (first reported in 2009), 92 reports of 5-MeO-AMT (first reported in 2003), 348 reports of 5-MeO-MiPT (first reported in 2004), 17 reports of 5-MeO-DET (first reported in 2006), and 25 reports of DiPT (first reported in 2003).⁴

6. What, if any, Risk There is to the Public Health:

HHS indicates that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT pose a risk to public health due to their hallucinogenic properties that usually occur quickly (often between 5-15 minutes, dependent on the route of administration) after ingestion and may cause impairing effects on the user’s judgment and lead to dangerous behavior. The risks could be to the individual user or to the community, especially when the user is operating a motor vehicle. Several adverse effects were reported in animal studies and in humans from Internet forums for all five tryptamines (see Factor 2). HHS also cited published and anecdotal reports that described the adverse effects of these five hallucinogens including agitation, confusion, psychological distress for all five substances, and death in the case of 5-MeO-AMT. It is unclear what role 5-MeO-AMT played in the death. The toxicology report also reported alcohol and the presence of an antidepressant, bupropion. Users of 4-OH-DiPT reported that the hallucinations were intense and the psychological and physiological effects were frightening or disturbing. A

⁴ NFLIS data were queried August 17, 2021, by date of submission.

non-lethal poisoning was reported in an adolescent after ingesting an alleged combination of 5-MeO-MiPT and harmaline, a CNS stimulant.

7. Its Psychic or Physiological Dependence Liability:

According to HHS, hallucinogens are not usually associated with physical dependence and the physiological dependence liability in animals or humans has not been reported in scientific and medical literature for these five substances. Thus, it is not possible at this time to determine whether 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT produce physiological dependence following acute or chronic administration. However, hallucinogen abusers may develop psychological dependence to these substances as evidenced by the continued use of these substances despite knowledge of the potential toxic and adverse effects.

The data on the drug discrimination studies conducted by the National Institute on Drug Abuse, cited in HHS reviews and later published, show that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT share discriminative stimulus effects with other schedule I hallucinogens: 4-OH-DiPT fully substitutes for DOM and LSD; 5-MeO-AMT partially substitutes for LSD and DMT; 5-MeO-MiPT fully substitutes for DOM; 5-MeO-DET fully substitutes for DMT; and DiPT fully substitutes for DOM and DMT. DEA adds that LSD, DOM, and MDMA fully substitute for DiPT-trained discriminative stimulus effects, confirming that DiPT has hallucinogenic effects similar to other schedule I hallucinogens.

8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:

4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not immediate precursors of a substance already controlled under the CSA as defined by 21 U.S.C. 802(23).

Conclusion:

Based on consideration of the scientific and medical evaluation and accompanying recommendations of HHS, and on DEA's consideration of its own eight-factor analysis, DEA finds that these facts and all relevant data constitute substantial evidence of potential for abuse of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT. As such, DEA hereby proposes to schedule 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT as controlled substances under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the former Assistant Secretary and review of all other available data, the Administrator, pursuant to 21 U.S.C. 812(b)(1), finds that:

(1) 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT elicit pharmacological effects qualitatively similar to those of schedule I hallucinogens (e.g., DOM, LSD, DMT, DET). These effects are marked by hallucinations and CNS stimulation. Law enforcement reported a number of encounters of 5-MeO-AMT and DiPT beginning in 2003, 5-MeO-MiPT beginning in 2004, 5-MeO-DET beginning in 2006, and 4-OH-DiPT beginning in 2009.

The available data indicate that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have high potential for abuse that is similar to that of other schedule I tryptamine hallucinogens DET (5-MeO-AMT) and DMT (5-MeO-DET, 5-MeO-MiPT, and DiPT), the phenethylamine hallucinogen DOM (4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT, and DiPT), and the ergotamine hallucinogen LSD (5-MeO-AMT, 4-OH-DiPT, 5-MeO-DET, 5-MeO-MiPT).

(2) 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT are not legally marketed in the U.S. They lack current marketing approval under new drug

applications, abbreviated new drug applications, or investigational use under an active investigational new drug application. There is no evidence that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have a currently accepted medical use in treatment in the U.S.⁵

(3) Because 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have no approved medical use and have not been thoroughly investigated as new drugs, their safety for use under medical supervision is not determined. Thus, there is a lack of accepted safety for use of these substances under medical supervision.

Based on these findings, the Administrator concludes that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT warrant control in schedule I of the CSA. More precisely, because of their hallucinogenic effects, and because they may produce hallucinogenic-like tolerance and dependence in humans, DEA proposes to place 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT, including their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical description, in 21 CFR 1308.11(d) (the hallucinogenic substances category of schedule I).

Requirements for Handling 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT

If this rule is finalized as proposed, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT would be subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution,

⁵ Although there is no evidence suggesting that 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT have a currently accepted medical use in treatment in the United States, it bears noting that a drug cannot be found to have such medical use unless DEA concludes that it satisfies a five-part test. Specifically, with respect to a drug that has not been approved by FDA, to have a currently accepted medical use in treatment in the United States, all of the following must be demonstrated: i. the drug's chemistry must be known and reproducible; ii. there must be adequate safety studies; iii. there must be adequate and well-controlled studies proving efficacy; iv. the drug must be accepted by qualified experts; and v. the scientific evidence must be widely available. 57 FR 10499 (1992), *pet. for rev. denied*, *Alliance for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994).

reverse distribution, import, export, research, conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses), or who desires to handle, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT would be required to be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312, as of the effective date of a final scheduling action. Any person who currently handles 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT, and is not registered with DEA, would need to submit an application for registration and may not continue to handle 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT as of the effective date of a final scheduling action, unless DEA has approved that application for registration pursuant to 21 U.S.C. 822, 823, 957, 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Any person unwilling or unable to obtain a schedule I registration would be required to surrender or transfer all quantities of currently held 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT to a person registered with DEA before the effective date of a final scheduling action, in accordance with all applicable Federal, State, local, and tribal laws. As of the effective date of a final scheduling action, 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT would be required to be disposed of in accordance with 21 CFR part 1317, in addition to all other applicable Federal, State, local, and tribal laws.

3. *Security.* 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT would be subject to schedule I security requirements for DEA registrants and would need to be handled and stored pursuant to 21 U.S.C. 823 and in accordance with

21 CFR 1301.71 through 1301.76 as of the effective date of a final scheduling action.

Non-practitioners handling 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT would also need to comply with the employee screening requirements of 21 CFR 1301.90 through 1301.93.

4. *Labeling and Packaging.* All labels and labeling for commercial containers of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT would need to be in compliance with 21 U.S.C. 825, and be in accordance with 21 CFR part 1302, as of the effective date of a final scheduling action.

5. *Quota.* Only registered manufacturers would be permitted to manufacture 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303, as of the effective date of a final scheduling action.

6. *Inventory.* Every DEA registrant who possesses any quantity of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT on the effective date of the final rule would need to take an inventory of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and/or DiPT on hand at that time, pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (d).

Any person who registers with DEA on or after the effective date of the final scheduling action would be required to take an initial inventory of all stocks of controlled substances (including 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and/or DiPT) on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (b).

After the initial inventory, every DEA registrant would be required to take a new inventory of controlled substances (including 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT,

5-MeO-DET, and/or DiPT) on hand every two years, pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

7. *Records and Reports.* Every DEA registrant would be required to maintain records and submit reports with respect to 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, DiPT, or products containing 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and/or DiPT pursuant to 21 U.S.C. 827 and in accordance with 21 CFR 1301.74(b) and (c) and parts 1304, 1312, and 1317, as of the effective date of a final scheduling action. Manufacturers and distributors would need to submit reports regarding these substances to the Automation of Reports and Consolidated Order System pursuant to 21 U.S.C. 827 and in accordance with 21 CFR parts 1304 and 1312, as of the effective date of a final scheduling action.

8. *Order Forms.* Every DEA registrant who distributes 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT would be required to comply with the order form requirements, pursuant to 21 U.S.C. 828, and 21 CFR part 1305, as of the effective date of a final scheduling action.

9. *Importation and Exportation.* All importation and exportation of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT would need to be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312, as of the effective date of a final scheduling action.

10. *Liability.* Any activity involving 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT not authorized by, or in violation of, the CSA or its implementing regulations would be unlawful, and could subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 and 13563 (Regulatory Planning and Review; Improving Regulation and Regulatory Review)

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures performed “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget pursuant to section 3(d)(1) of Executive Order (E.O.) 12866 and the principles reaffirmed in E.O. 13563.

Executive Order 12988, Civil Justice Reform

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of E.O. 12988, to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

Executive Order 13132, Federalism

This proposed rulemaking does not have federalism implications warranting the application of E.O. 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the National Government and the States, or the distribution of power and responsibilities among the various levels of government.

Executive Order 13175, Consultation and Coordination with Indian Tribal Governments

This proposed rule does not have tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

Paperwork Reduction Act of 1995

This proposed action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3521).

Regulatory Flexibility Act

The Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 601-612), has reviewed this proposed rule, and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities.

DEA proposes placing the substances 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-methyltryptamine (5-MeO-AMT), 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (5-MeO-MiPT), 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET), and *N,N*-diisopropyltryptamine (DiPT), including their salts, isomers, and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation, in schedule I of the CSA. If finalized, this action would impose regulatory controls and administrative, civil, and/or criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities, or chemical analysis with, or possess), or propose to handle 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, or DiPT.

There appear to be no legitimate sources for 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT as marketed drugs and no accepted medical use in the United States, but DEA notes that these substances are available for purchase from legitimate suppliers for scientific research. There is no evidence of significant diversion of 4-OH-DiPT, 5-MeO-AMT, 5-MeO-MiPT, 5-MeO-DET, and DiPT from legitimate suppliers.

DEA has identified 31 domestic suppliers of one or more of the following substances: 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-methyltryptamine (5-MeO-AMT), 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (5-MeO-MiPT), 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET), and *N,N*-diisopropyltryptamine (DiPT). Thirty (30) of the 31 domestic suppliers are not registered with DEA to handle controlled substances. The one registered supplier is already registered with DEA and

has all security and other handling processes in place, resulting in minimal impact to this supplier. Therefore, the remaining 30 non-registered domestic suppliers are affected. Since the vast majority of DEA registrants are small entities or are employed by small entities, all 30 affected suppliers are assumed to be small entities. It is impossible to know how much 4-hydroxy-*N,N*-diisopropyltryptamine (4-OH-DiPT), 5-methoxy-*alpha*-methyltryptamine (5-MeO-AMT), 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (5-MeO-MiPT), 5-methoxy-*N,N*-diethyltryptamine (5-MeO-DET), and *N,N*-diisopropyltryptamine (DiPT) are distributed by these suppliers. It is common for suppliers to have items on their catalog while not actually having any material level of sales. Based on the discussion above, DEA believes any quantity of sales from these distributors for legitimate purposes is minimal. Therefore, these suppliers are expected to remove the product from their catalog rather than incur the cost of obtaining a DEA registration and physical security for products with minimal sales. Therefore, DEA estimates the cost of this rule, in form of lost sales, if any, on the affected small entities is minimal. DEA welcomes any public comment regarding this estimate.

Because of these facts, this proposed rule will not, if promulgated, result in a significant economic impact on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

On the basis of information contained in the “Regulatory Flexibility Act” section above, DEA has determined pursuant to the Unfunded Mandates Reform Act (UMRA) of 1995 (2 U.S.C. 1501 *et seq.*) that this proposed action would not result in any Federal mandate that may result “in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any 1 year” Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA proposes to amend 21 CFR part 1308 as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES

1. The authority citation for 21 CFR part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. In § 1308.11, as proposed to be amended at 86 FR 16553 (March 30, 2021), 86 FR 37719 (July 16, 2021), and 86 FR 69187 (December 7, 2021), add paragraphs (d)(101) through (105) to read as follows:

§ 1308.11 Schedule I.

* * * * *

(d) * * *

(101) 4-hydroxy-*N,N*-diisopropyltryptamine (other names: 4-OH-DiPT; 3-(2-(diisopropylamino)ethyl)-1*H*-indol-4-ol)7516

(102) 5-methoxy-*alpha*-methyltryptamine (Other names: 5-MeO-AMT; 1-(5-methoxy-1*H*-indol-3-yl)propan-2-amine).....7506

(103) 5-methoxy-*N*-methyl-*N*-isopropyltryptamine (Other names: 5-MeO-MiPT; *N*-(2-(5-methoxy-1*H*-indol-3-yl)ethyl)-*N*-methylpropan-2-amine).....7512

(104) 5-methoxy-*N,N*-diethyltryptamine (Other names: 5-MeO-DET; *N,N*-diethyl-2-(5-methoxy-1*H*-indol-3-yl)ethanamine)7525

(105) *N,N*-diisopropyltryptamine (Other names: DiPT; *N*-(2-(1*H*-indol-3-yl)ethyl)-*N*-isopropylpropan-2-amine)7522

* * * * *

Anne Milgram,
Administrator.

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